NUTRIENTS AND THE INNATE IMMUNE RESPONSE

K. M. Moyes
Department of Animal and Avian Sciences
University of Maryland

INTRODUCTION

Several researchers have focused on the influence of stress and physiological state on immune system function (Ingvartsen and Moyes, 2013). This presentation will primarily focus on the effect of stress and dietary vitamin/mineral supplementation on the innate immune response with a focus on the benefits of dietary chromium on the innate immune response. The immune system is defined as host resistance to invading microorganisms. The immune system is comprised of the innate and adaptive immune response. The innate immune response is non-specific and consists primarily of phagocytic cells such as resident macrophages and circulating neutrophils. The primary functions of the innate immune response are to detect invading microorganisms, recruit circulating neutrophils to phagocytose (i.e. engulf) and kill invading microorganisms. Resident macrophages also bridge the innate with the adaptive immune response via antigen presentation for the priming of T cells (Rainard and Riollet, 2006). The adaptive immune response is specific to invading microorganisms and primarily consists of lymphocytes. Lymphocytes consists of T (i.e. cytotoxic or helper) and B (i.e. antibodies) lymphocytes. This review will focus on the innate immune response.

IMPACT OF STRESS ON IMMUNE FUNCTION

Any stressor can impact the immune response. The major stressors that impact dairy production include heat, transportation, crowding as well as physiological stressors such as parturition (Ingvartsen and Moyes, 2013). Although many different stressors can impact dairy management and production, this presentation will primarily focus on the stressors associated with the transition period, i.e. ± 3 weeks relative to parturition (Drackley, 1999).

The transition period is considered the most critical time period regarding its influence on health and immune function. During this time, complex changes in the endocrine, neurological, digestive and immune systems occur that increase risk for disease (Ingvarsten and Moyes, 2015). As a result, ~75% of all diseases occur during the transition period. Mortality rates are also high for cows in early lactation with 50% of deaths occurring by 30 days after calving (Dechow and Goodling, 2008; Thomsen et al., 2006). Natural immunosuppression has been observed at this time that partly explains the decreased immune system function and risk of disease (Burton et al., 2005).

Natural immunosuppression that occurs around the transition period is multifactorial. Major factors associated with immunosuppression include, but are not limited to, endocrine changes, milk yield, management and genotype. All are associated

with increasing risk of disease. Mastitis, defined as an inflammation of mammary gland, occurs more frequently at the time of parturition and is the most common and most economically significant disease affecting dairy cattle (Cha et al., 2011). The decrease in economic returns and animal welfare can be partly associated with the rise in milk somatic cell count (~90% neutrophis), i.e. the primary indicator of mastitis (Sordillo et al., 1997). Although the immune response to invading microorganisms in the mammary gland has been well-documented, the metabolic response including the utilization of nutrients by phagocytic cells has received little attention. Identifying the metabolic response and the utilization of nutrients during the transition period may partly explain the high risk for disease at this time.

NUTRIENT UTILIZATION DURING INFLAMMATION

Studies of fuel use have indicated that 1) only 5% of glucose is completely oxidized via the Krebs' cycle and the rest is either directed towards the pentose phosphate pathway for the generation of reducing equivalents required for phagocytoses or is converted to lactate due to the low oxygen availability in immune cells; 2) glutamine is the preferred amino acid utilized by phagocytes, with ~74% of glutamine being completely oxidized; 3) fatty acids, such as oleate, are primarily incorporated into cellular lipids; and 4) ketone bodies are not utilized as an energy source by phagocytic cells (Ingvartsen and Moyes, 2013). However, the partitioning and benefits of other nutrients, such as chromium, by bovine phagocytic cells is currently unknown and warrants further investigation.

IMPACT OF VITAMINS/MINERAL SUPPLY ON IMMUNE RESPONSE

Vitamin E as one of the most important antioxidants extensively studied in humans and animals. Previous studies have shown that inadequate vitamin E concentration may partly explain the increased risk of metabolic and infectious diseases in dairy cows shortly after calving (Heinrichs et al., 2009). Selenium, a mineral primarily found in soil, also has antioxidant properties. Increasing dietary vitamin E with or without selenium may improve the innate immune response (Hogan et al., 1990). Growing evidence suggests that additional nutrients can alter the immune response for dairy cows during the transition period.

Dietary chromium supplementation primarily modulates the host response to insulin (Vincent, 2004). Few researchers have examined the effect of dietary chromium on the immune response, especially for dairy cows during the transition period. Researchers have shown that chromium supplementation improves insulin response, energy metabolism, dry matter intake and milk yield for lactating dairy cows (Hayirli et al., 2001; Soltan, 2010). Regarding the innate immune response, chromium supplementation has been shown to improve monocyte and neutrophil function (Burton et al., 1993; Yasui et al., 2014) as well as the anti-inflammatory response for lactating cows experiencing heat stress (Zhang et al., 2014). Immune cells primarily use insulin independent glucose transporters, i.e. GLUT-1 and GLUT-3, yet insulin receptors have been identified on bovine immune cells (Nielsen et al., 2003). Although the function of

insulin receptors on bovine immune cells remains unknown, researchers theorize that the insulin receptors are involved in monocyte function such as neutrophil recruitment. The role of dietary chromium supplementation on insulin receptor signaling as well as the overall innate immune response for transition dairy cows, especially during mastitis, has not been elucidated and warrants further investigation.

SUMMARY AND CONCLUSION

In summary, most cows are immunosuppressed around calving, primarily attributed to changes in the endocrine, neurological, digestive, and immune systems. Nutrient supply can alter the immune response. For phagocytic cells, glucose enters either the pentose phosphate pathway or is converted to lactate. Immune cells primarily oxidized glutamine for energy in the citric acid cycle. To my knowledge, ketones are not utilized or produced by phagocytic cells and fatty acids can be incorporated into cellular lipids and have been shown to alter the immune response. Vitamins and minerals, such as vitamin E and selenium, improve the immune system response, especially during the transition period. Although few studies have investigated the effects of chromium on the immune response, results suggest that dietary chromium supplementation may benefit the innate immune response. In conclusion, the benefits of dietary chromium supplementation on the innate immune response for dairy cows and how this effect is altered by age, physiological state and stage of lactation is vital for the development of new management strategies that improve the immune response and reduce risk of disease during the transition period through dietary chromium supplementation.

ACKNOWLEDGMENTS

Data presented from the Moyes laboratory was supported by Kemin Industries (Des Moines, IA) and the Maryland Agricultural Experiment Station. For further information, contact Dr. Kasey Moyes at kmoyes@umd.edu.

REFERENCES

Burton, J. L., S. A. Madsen, L. C. Chang, P. S. Weber, K. R. Buckham, D. R. van, M. C. Hickey, and B. Earley. 2005. Gene expression signatures in neutrophils exposed to glucocorticoids: a new paradigm to help explain "neutrophil dysfunction" in parturient dairy cows. Vet. Immunol. Immunopathol. 105(3-4):197-219.

Burton, J. L., B. A. Mallard, and D. N. Mowat. 1993. Effects of supplemental chromium on immune responses of periparturient and early lactation dairy cows. J. Anim Sci. 71(6):1532-1539.

Cha, E., D. Bar, J. A. Hertl, L. W. Tauer, G. Bennett, R. N. Gonzalez, Y. H. Schukken, F. L. Welcome, and Y. T. Grohn. 2011. The cost and management of different types of clinical mastitis in dairy cows estimated by dynamic programming. J. Dairy Sci. 94(9):4476-4487.

Dechow, C. D., and R. C. Goodling. 2008. Mortality, culling by sixty days in milk, and production profiles in high- and low-survival Pennsylvania herds. J. Dairy Sci. 91(12):4630-4639.

Drackley, J. K. 1999. Biology of dairy cows during the transition period: the final frontier? J. Dairy Sci. 82(11):2259-2273.

Hayirli, A., D. R. Bremmer, S. J. Bertics, M. T. Socha, and R. R. Grummer. 2001. Effect of chromium supplementation on production and metabolic parameters in periparturient dairy cows. J. Dairy Sci. 84(5):1218-1230.

Heinrichs, A. J., S. S. Costello, and C. M. Jones. 2009. Control of heifer mastitis by nutrition. Vet Microbiol. 134(1-2):172-176.

Hogan, J. S., K. L. Smith, W. P. Weiss, D. A. Todhunter, and W. L. Schockey. 1990. Relationships among vitamin E, selenium, and bovine blood neutrophils. J. Dairy Sci. 73(9):2372-2378.

Ingvarsten, K. L., and K. M. Moyes. 2015. Factors contributing to immunosuppression in the dairy cow during the transition period. Jpn. J. Vet. Res. 63 (Suppl. 1):S15-S24.

Ingvartsen, K. L., and K. M. Moyes. 2013. Nutrition, immune function and health of dairy cattle. Animal 7 (Suppl 1):112-122.

Nielsen, L., C. Rontved, M. O. Neilsen, L. R. Norup, and K. L. Ingvartsen. 2003. Leukocytes from heifers at different ages express insulin and insulin-like growth factor-1 (IGF-1) receptors. Domest. Anim Endocrinol. 25(2):231-238.

Rainard, P., and C. Riollet. 2006. Innate immunity of the bovine mammary gland. Vet. Res. 37(3):369-400.

Soltan, M. A. 2010. Effect of dietary chromium supplementation on productive and reproductive performance of early lactating dairy cows under heat stress. J. Anim Physiol Anim Nutr. (Berl) 94(2):264-272.

Sordillo, L. M., K. Shafer-Weaver, and D. DeRosa. 1997. Immunobiology of the mammary gland. J. Dairy Sci. 80(8):1851-1865.

Thomsen, P. T., A. M. Kjeldsen, J. T. Sorensen, H. Houe, and A. K. Ersboll. 2006. Herd-level risk factors for the mortality of cows in Danish dairy herds. Vet. Rec. 158(18):622-626.

Vincent, J. B. 2004. Recent advances in the nutritional biochemistry of trivalent chromium. Proc. Nutr. Soc. 63(1):41-47.

Yasui, T., J. A. McArt, C. M. Ryan, R. O. Gilbert, D. V. Nydam, F. Valdez, K. E. Griswold, and T. R. Overton. 2014. Effects of chromium propionate supplementation during the periparturient period and early lactation on metabolism, performance, and cytological endometritis in dairy cows. J. Dairy Sci. 97(10):6400-6410.

Zhang, F. J., X. G. Weng, J. F. Wang, D. Zhou, W. Zhang, C. C. Zhai, Y. X. Hou, and Y. H. Zhu. 2014. Effects of temperature-humidity index and chromium supplementation on antioxidant capacity, heat shock protein 72, and cytokine responses of lactating cows. J. Anim Sci. 92(7):3026-3034.